REMARKS

Claims 1-20 stand cancelled and claims 21-29 are pending. Claim 29 has been amended merely to correct an improper dependency. No new matter has been introduced by the instant amendments; support therefor being found in the claims as originally filed and in the specification.

Referring now to the Office Action, claim 29 was rejected under 35 USC §112, 2nd paragraph, for depending upon certain claims which were previously cancelled. Accordingly, that informality has been obviated by virtue of the within amendment to claim 29. Withdrawal of the rejection is therefore requested.

The remaining rejections are summarized as follows.

Claims 21-26 and 28-29 stand rejected under 35 USC §103(a) over US Patent Application 11/097,994 (the '994 application) in view of Carloni et al.

Claims 23 and 26-27 stand rejected under 35 USC §103(a) over the '994 application in view of Aoki et al. (1998).

The rejections are traversed. The cited documents, even in combination, do not teach or suggest Applicant's claimed invention in any manner sufficient to sustain a rejection under 35 USC §103.

Referring first to the '994 application, the Office Action draws attention to paragraphs 27, 28, 91, 100, 109, 120 and Figure 1 therein. The Office Action goes on to state that cells are attached or immobilized to a semipermeable membrane, including a hollow fiber filter or porous hollow microballoon housed within the bioreactor (making particular reference to the '994 application at paragraphs 27 and 28).

It is noted, however, that paragraphs 27 and 28 of the '994 application do not describe the system represented in Figure 1. Rather, as that reference is understood, the discussion is related to a method for the filtration of medium and cells of the prior art disclosed in the '994 application.

Additionally, particular attention is directed to paragraphs 110 to 120 of the '994 application which describe in detail the bioreactor system disclosed in Figure 1 of that application. According to the description provided therein, the bioreactor system of the '994 application consists of a cell culture loop 100, a medium replenishment loop 200 and dialysis device 300, and cells are proliferated in a bioreactor 110 in which cells are not immobilized on a porous carrier. Further, dialysis device 300 is merely for the filtration of medium from the cell culture provided from bioreactor 110 and filtrated cells are returned through port 113 to the bioreactor 110. Thus, the dialysis device 300 of the '994 application is not a radial flow bioreactor.

In contrast, the bioreactor system used in the present invention comprises a culture vessel having a porous carrier capable of immobilizing a human hepatocyte thereon which can generate a continuous stream of a liquid medium in the vessel. According to the present invention, a human hepatocyte is immobilized and proliferated on the porous carrier in the culture vessel by generating therein the continuous stream of liquid medium; it is then infected with a hepatitis C virus by adding the hepatitis C virus to the stream of liquid medium followed by proliferating the hepatitis C virus in the human hepatocyte by maintaining the continuous stream of liquid medium.

Accordingly, the bioreactor system disclosed in the '994 application is quite distinct from that used in the present invention.

Carloni et al. cannot remedy the deficiencies of the '994 application. Indeed, that reference merely provides culture conditions required for hepatitis C virus in a human hepatocyte cell line.

Aoki et al. is also deficient and adds little to the combined disclosure. Indeed, Aoki et al. merely teaches an established human cell line FLC-4.

Reconsideration and withdrawal of the rejections are therefore requested. For instance, it is well-known that to establish a *prima facie* case of obviousness, three basic criteria must be met: (1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary

skill in the art, to modify the reference or to combine reference teachings; (2) there must be a reasonable expectation of success; and (3) the prior art reference(s) must teach or suggest all the claim limitations. The teaching or suggestion to make the claimed combination and the reasonable expectation of success must both be found in the prior art, and not based on applicant's disclosure. *In re Vaeck*, 947 F.2d 488, 20 USPQ2d 1438 (Fed. Cir. 1991). See MPEP § 2143.

There is no suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the cited references to make the claimed invention, nor is there a reasonable expectation of success. The cited references do not teach or suggest the features of the present invention.

Further rebutting any *prima facie* case of obviousness which may be contended, the bioreactor system used in the present application has received significant acclaim from those skilled in the art because it mimics the internal liver for the proliferation of a human hepatocyte. Indeed, Applicant wishes to note that the inventor of the present invention, Dr. Seishi Nagamori, was awarded an ASAIO Fellowship from the American Society for Artificial Internal Organs at the ASAIO 51st Annual Conference 2005 held in Washington, D.C., for his work entitled "Expression of CYP3A4 by an Immobilized Human Hepatocyte Line Using a Radial Flow Bioreactor".

In view of the above amendments and remarks, Applicant believes the pending application is in condition for immediate allowance.

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Respectfully submitted,

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